CASE REPORTS

"Q" Fever Hepatitis

Report of a Case in the Mojave Desert

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THE LITERATURE in recent years has brought to light the numerous diseases of protean manifestation, not the least among which is "Q" fever, that are caused by the rickettsia Coxiella burnetii. "Q" fever was originally described as a disease distinct from, but often similar in its manifestations to, typhus fever and leptospirosis. In the past few years the literature, particularly from California, Australia and Canada,[10] has been focusing upon liver involvement in this disease.

The following is a case report of anicteric hepatitis occurring in one of the military personnel at George Air Force Base, Victorville, California, in the upper Mojave Desert. There has never been such a case reported before in this community of 80,000 people in the Victor Valley.

Report of a Case

A 33-year-old staff sergeant, USAF, was well until 9 June 1965, when a fever of 37.2°C (99°F), non-productive cough, sore throat and headache developed. The patient said he had not been out of the state for two years, had been around no one else with similar symptoms and kept no pets. He had received no injections or transfusions in the preceding 18 months. For two days before visiting the clinic, he had noted "dark yellow, almost brownish" urine. Physical examination in the clinic was within normal limits except for mild, right upper quadrant tenderness. The liver was not palpably enlarged. Urinalysis was essentially normal and the urine was yellow. Laboratory studies were ordered and the patient was treated with expectorants for a probable viral infection of the upper respiratory tract.

The patient returned in four days, feeling better, although cough, sore throat, and headache still remained. He was afebrile. On physical examination no changes were noted.

The patient returned 17 June, stating that his headache had subsided. He then said that he had begun to have a distaste for cigarettes. With the laboratory studies received (Table 1), it was felt that the patient had anicteric hepatitis, probably viral. This concept changed with the results of the complement fixation studies for "Q" fever, which were diagnostic.

The patient was admitted for liver biopsy on 21 June. At this time he was asymptomatic. An x-ray film of the chest showed no abnormality. A liver biopsy specimen was sent to March AFB, California, where the interpretation was: "There are variations of liver cells as to their nuclear size. The liver cells contain increased amounts of hemisiderin and bile. Occasional polymorphonuclear cells are present in the sinusoids." The pathologist stated the findings were consistent with hepatitis. It should be noted bile was never found in the urine. Since discharge the patient has remained asymptomatic.

Comment

The case was one of anicteric hepatitis caused by "Q" fever. There was no evidence of pneumonitis. How the patient contracted the disease still remains obscure. He had no involvement with horses, sheep

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Submitted 10 October 1966, Revised 31 March 1967.

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TABLE 1.—*Laboratory Findings in a Case of "Q" Fever Hepatitis*

	10 June	14 June	17 June	21 June	7 July	21 July	16 Sep.	5 Oct.
Leukocytes (per cu mm)	6,500	6,700						
Segmented	75%	67%						
Bands		} 2%						
Eosinophiles								
Basophiles								
Atypical		10%						
Lymphocytes	25%	28%						
Monocytes		3%						
Hematocrit	41%	39%						
Sedimentation rate (mm/hr)	18	24						
Bromsulphthalein							1% (45 min.)	
Serum glutamic oxaloacetic transaminase (Babson units)	64	34	84		14	14	15	
Serum glutamic pyruvic transaminase		126	126		18		0	
Alkaline phosphatase (Bodansky units)		3	6		4	4	4	
Bilirubin (mg per 100 ml):								
Total			0.5		0.5	0.3	0.4	
Direct			0.2		0.05	0.1	0.3	
Heterophile agglutination		neg.						
Cold agglutinins			neg.					
Febrile agglutinins				norm.				
Lupus erythematous preparation			neg.					
Complement fixation for "Q" fever*				1:160	1:80			1:10
Albumin:Globulin ratio					3.4:4.0	4.4:2.6	4.6:3.0	
Thymol turbidity (units)						8	6.3	
Throat culture						neg.		

*Done at Sixth Army Laboratory, Fort Baker, California.

or cattle. His only household pet was a dog which had died in March 1965 from "heart worms." He had been at George AFB, Victorville, for two years and had not left the local area in that time.

Complement fixation studies on his wife and children for "Q" fever were negative. There have been no reported cases in humans or animals in this area of the Victor Valley.

There is real possibility that there was transient hyperbilirubinemia and biliuria at the onset of what subsequent studies suggested was an anicteric form of hepatitis. However, the patient was never noted to be jaundiced by his friends or family and no previous blood studies had been done.

Originally "Q" fever was thought of as a condition in which the patient had a high fever, sometimes relapsing in nature, occurring acutely, accompanied by severe cephalgia, a slow pulse rate and no other obvious localizing symptoms. Derrick[5] said that "Q" fever is to be distinguished from influenza by the mildness or absence in the former of localized respiratory symptoms, . . . by the comparatively slow pulse rate and by the sporadic distribution." Subsequent to this, however, it was realized that the respiratory complaints and findings typical of pneumonia were relatively common in "Q" fever.[1]

In a review of cases in California, Clark and coworkers[4] noted that hepatomegaly and liver tenderness were surprisingly common, occurring in 11 per cent and 7 per cent respectively in a series of 180 cases. However, the occurrence of hepatitis[8] and especially anicteric hepatitis[12] as the only manifestation of the disease has been realized more frequently only recently.

Symptomatologically, "Q" fever is characterized primarily by a severe generalized headache. Conjunctival injection is frequently seen; however, only about 10 per cent of patients have a diffuse macular rash. Fever, malaise, anorexia, cough and pleuritic pain are fairly common symptoms. Nuchal rigidity, abdominal pain, vomiting, diarrhea and scrotal pain sometimes occur, but not often.[1]

Physical findings are often scant. Conjunctival injection may be seen, as well as pleural friction rubs and rales when there is pulmonary involvement. Scleral icterus, hepatomegaly and liver tenderness are present in 10 to 15 per cent of cases. In some surveys the incidence of splenomegaly was 5 per cent.[4] Abdominal tenderness and nuchal

rigidity are unusual. Other unusual findings are cardiac murmur, reflex changes, apathy and confusion and scrotal swelling and tenderness.

There have been many descriptions of the pathological changes that occur in this disease, most interest centering around the liver biopsy. Geistl[8] described numerous focal lesions with involved liver cells showing an intense acidophilic vacuolated cytoplasm. However, the acidophilic hyaline bodies seen in acute viral hepatitis were not seen. No vascular lesions were seen and Kupfer-Stern cells were prominent. There was an infiltrate of round cells with eosinophils and an occasional polymorphonuclear leukocyte. No giant or epithelioid cells were found. Geistl said: "The lack of fibroblasts and the scarcity of inflammatory cells set [the lesions] apart from true granulomas."[10]

Picchi and Nelson reported three cases from the Oakland, California area in which the characteristic pathologic feature of liver biopsy was multinucleated giant cells giving a diffuse granulomatous appearance. They suggested that "Q" fever be considered subsequently in the differential diagnosis of diffuse granulomatous diseases.[8]

Edmundson[3] noted the granulomatous changes in the liver and in addition he suggested a sequence of changes characterizing "Q" fever hepatitis as follows: Kupfer cell infection and proliferation gives rise to multinucleated cells; next the sinusoidal wall fragments and swells and this is followed by an infiltrate of neutrophils, round cells and a few eosinophils. Parenchymal cells may or may not undergo necrosis before healing occurs. Characteristic eosinophilic changes in the vascular walls were described. Edmundson also commented on hepatic fundal changes that were stated to be suggestive of "Q" fever.

The differential diagnosis when "Q" fever is considered is becoming longer with every new report. Already it includes infectious hepatitis, infectious mononucleosis, primary atypical pneumonia, typhoid fever, typhus fever, leptospirosis, undulant fever,[9] acute anemia[4] and diffuse granulomatous diseases.[8,12]

Laboratory findings are not unique. Hypocholesterolemia, false positive Kolmer reactions and normochromic normocytic anemia have been mentioned.[4,11,12] The diagnosis is made serologically. A complement fixation titer of greater than 1:16 is considered diagnostic by Babudieri.[2] Clark and coworkers[4] listed in their criteria a titer of 1:32 or greater as significant.

The prognosis is usually excellent. Patients with hepatic involvement, however, usually have greater morbidity; fatal cases have been reported.[3]

The need to establish *Coxiella burnetii* as the etiologic agent is important for in many cases there is good response to broad-spectrum antibiotics. Chloramphenicol has been found to be the most effective.[8,12]

Summary

A case has been presented of a 33-year-old serviceman with "Q" fever presenting as anicteric hepatitis. A brief review of the clinical and pathological findings is presented.

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